REMARKS

Claims 1-8 are rejected under 35 U.S.C. §101 as directed to non-statutory subject matter. Claims 1-8 are further rejected under 35 U.S.C. §112, second paragraph, as being indefinite for a reason specified by the Examiner. Claims 1-5 and 8 are rejected under 35 U.S.C. §102(b) and (e)(2) as being clearly anticipated by U.S. Patent 5,353,236 to Subbiah.

Applicant respectfully traverses the rejection of Claims 1-8 under 35 U.S.C. §112, second paragraph, as being indefinite for reciting "a plurality of reflections." No specific number of reflections are taught in applicant's specification since persons of ordinary skill in the art select some number of reflections depending on a desired resolution, as illustrated in Subbiah at Col. 8, lines 1-9. Indeed, an electron density map can be constructed from a single reflection (see, e.g., Subbiah at Col. 4, 29-32) so that the claimed process could be practiced with as few as two reflections. The exact number of reflections will simply be determined by a resolution determined by the experimenter. Applicant's process provides a modified first electron density map by recognizing features in an initial map that yield expected electron density distributions, which are used to obtain crystallographic phase probability distributions. This is done for all of the plurality (at least two) of reflections, where the most probable crystallographic phases are selected from the resulting maps to provide an updated electron density map. No undue experimentation is required for this determination since a large number of reflections are conventionally recorded, as illustrated by Subbiah.

Applicant respectfully traverses the rejection of the claims under 35 U.S.C. §101 as directed to non-statutory subject matter. The Examiner remarks that the process manipulates electron density data "without resulting in any physical transformation outside of a computer or other computational device." As noted in MPEP 2106.IV.B.2.(b).(i), a process is clearly statutory "it if requires physical acts to be performed outside the computer . . . . But, "[i]f a claim does not clearly fall into one or both of the safe harbors, the claim may still be statutory if it is limited to a practical application in the technological arts." The next section of MPEP provides an example:

" . . .a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing a mathematical algorithm is statutory." Applicant's claimed process is the application of mathematical algorithms to modify "an electron density map of an experimental crystal structure," as recited in the preamble of Claim 10. This is clearly a "practical application in the technological arts" and constitutes statutory subject matter under 35 U.S.C §101. To more clearly recite this function, the step of forming a final electron density map from the final set of crystallographic phases is recited. The rejection of Claims 10-14 as being directed to nonstatutory subject matter should be withdrawn.

Finally, applicant respectfully traverses the rejections of Claims 1-5 and 8 under 35 U.S.C. §102(b) and (e)(2) as being clearly anticipated by U.S. Patent 5,353,236 to Subbiah. Subbiah begins with measured amplitudes of structure factors, but no phase information, and yields phases and an electron density map. See, e.g., Col. 4, lines 27-35:

> The process is started with a low-resolution envelope of the macromolecular crystal. That envelope is used to obtain the phrase of the structure factor for one (or a few) low-resolution reflections. The phase of that structure factor is then used to construct a new, higher resolution envelope which is, in turn, used to calculate the phase for a higher resolution reflection so that an even higher resolution envelope can be constructed.

In another aspect, Subbiah finds arrangements of atomic scatterers that lead to calculated amplitudes of structure factors that are maximally consistent with measured amplitudes of structure factors.

In contrast, the claimed process of the present invention begins with measured amplitudes of structure factors and a set of starting phases are selected, not calculated from an envelope, and yields estimates of phases and an electron density map that have reduced bias. The input phases are adjusted to yield a map that has characteristics anticipated from the map features, but that were not used in constructing the initial estimates of phases.

To anticipate applicant's claimed invention, Subbiah must disclose every limitation in applicant's claimed process. Subbiah fails to disclose the following claim process steps:

(b) selecting a starting set of crystallographic phases to combine with the observed structure factor amplitudes to form a first set of structure factors;

(d) identifying features of the first electron density map to obtain expected distributions of electron density;

(e) making a comparison between the first electron density map and the expected distribution of electron density;

(f) estimating how changes in the crystallographic phase of a reflection *k* affect the comparison;

(g) establishing crystallographic phase probability distributions from the comparisons for the possible crystallographic phases of reflection *k*;

(h) repeating steps (c) through (g) as *k* is indexed through all of the plurality of reflections;

(i) deriving an updated electron density map using crystallographic phases determined to be most probable from the crystallographic phase probability distributions for each one of the reflections;

(j) repeating steps (d) through (i) to obtain a final set of crystallographic phases with minimum bias from known electron density maps.

Subbiah, Col. 10, line 48, through Col. 21, line 38, referenced by the Examiner to show details of the Subbiah improvement process, teaches only moving scatterers about the map grid, calculating the Fourier amplitudes as the scatterers are moved, and correlating the calculated amplitudes with experimental X-ray diffraction data. There is no teaching about establishing comparisons by altering possible crystallographic phases to establish crystallographic phase probability distributions.

SN S-96,583
Docket No. 10/017,643
In Response to Office Action dated September 24, 2003

Applicant respectfully asserts that Claims 1-8, as amended, are in condition for allowance. The Examiner is requested to allow Claims 1-8 and to pass this case to issue. Applicant's attorney would be pleased to discuss any of these matters with the Examiner if the Examiner considers such a discussion would assist in placing the case in condition for allowance.

Respectfully submitted,

Date: Dec. 16, 2003

Signature of Attorney

Reg. No. 28,351
Phone (505) 665-3112

Ray G. Wilson
Los Alamos National Laboratory
LC/IP, MS A187
Los Alamos, New Mexico 87545